

# First-Line Inhaled Steroids for Pediatric Asthma Gain Support

BY BRUCE JANCIN  
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KEYSTONE, COLO. — Clinically meaningful indicators of asthma control in children with mild to moderate persistent asthma improved significantly more with an inhaled corticosteroid than with a leukotriene inhibitor in a randomized, double-blind crossover study, Dr. Joseph D. Spahn reported at a meeting sponsored by the National Jewish Medical and Research Center.

The number of days per week in which asthma was under control was significantly greater and the need for supplemental albuterol less with fluticasone compared with montelukast in the 16-week trial.

Greater improvement also was found in morning peak expiratory flow and other measures of pulmonary response during fluticasone therapy, as well as in levels of inflammatory biomarkers, said Dr. Spahn of the Denver center.

He presented highlights of an analysis of key secondary end points in a National Heart, Lung, and Blood Institute-sponsored study involving 126 children aged 6-17 years. The primary study end point—the percentage of patients who responded to 8 weeks of therapy with at least a 7.5% increase in forced expiratory volume in 1 second (FEV<sub>1</sub>)—was previously re-

ported (J. Allergy Clin. Immunol. 2005;115:233-42).

The study has come under considerable criticism—legitimately, in Dr. Spahn's view, and he was a study coauthor—for this choice of a primary end point. Because the mean baseline FEV<sub>1</sub> was already 96% of predicted, a child had to have an on-treatment FEV<sub>1</sub> in excess of 100% to be classified as significantly improved. That's setting the bar very high, he said.

In all, 23% of the children met the primary end point while on fluticasone only, 5% on montelukast only, and 17% on both drugs.

The more recent analysis by Dr. Spahn and his colleagues looked at a broader range of clinical, pulmonary, and inflammatory responses to therapy (see box). Fluticasone consistently came out ahead, providing the first solid evidence-based support for current national and international guidelines that relied on expert opinion in recommending inhaled corticosteroids as the preferred first-line therapy for mild to moderate persistent asthma in children.

Predictors of a greater therapeutic response to fluticasone than to montelukast in terms of asthma control days per week included greater baseline albuterol use, more positive skin test responses, and higher levels of exhaled nitric oxide, a marker of airway inflammation (J. Allergy Clin. Immunol. 2006;117:45-52). ■

## Responses to Fluticasone and Montelukast

End Point	Baseline Mean	Adjusted Mean On Fluticasone	Adjusted Mean On Montelukast
Avg. no. of asthma control days/week	2.2	5.0	4.3
Albuterol puffs per week	7.5	3.1	4.4
Asthma control questionnaire score	0.96	0.59	0.76
Morning peak expiratory flow (L/min)	307.6	334.2	324.8
FEV <sub>1</sub> /forced vital capacity (%)	80.1	82.2	79.0
Exhaled nitric oxide (ppb)	39.5	20.6	30.9

Source: Journal of Allergy and Clinical Immunology

# Omalizumab Controls Severe Allergic Asthma

BY PATRICE WENDLING  
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MIAMI — Omalizumab maintained control of severe allergic asthma and reduced the need for inhaled corticosteroids during 3 years of treatment in an analysis of data from a 52-week open-label extension study.

The findings extend the results of previous studies by showing that asthma control and a favorable safety and tolerability profile were maintained during long-term treatment with the anti-IgE monoclonal antibody, Dr. Jacques Hébert and associates reported in a poster at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

The study was supported by Genentech Inc. and Novartis Pharmaceuticals Corp., which comarket omalizumab (Xolair). The drug gained federal approval in June 2003 for the treatment of moderate to severe asthma in patients age 12 years and older.

In the core 32-week study of 341 patients, omalizumab significantly reduced the use of inhaled corticosteroids and rescue medications while improving symptom scores and quality of life, compared with placebo. A first extension to this trial showed that these favorable efficacy and safety findings were sustained for a further 96 weeks of treatment.

In a second extension of the trial, researchers enrolled 178 patients, of whom 149 (84%) completed the study. Patients underwent a washout period of 12 weeks or more before receiving omalizumab subcutaneously at a dose of 0.016 mg/kg or more per IU/mL of IgE every 2 weeks or 4 weeks for up to 52 weeks. Mean forced expiratory volume in 1 second (FEV<sub>1</sub>) showed no decline between the start of the first extension (baseline) and week 52 of the second extension (2.24 L vs. 2.26 L). Good or excellent asthma control, based on the physician's overall assessment, was sustained from baseline to week 52 in 121 of the 149 (81%) patients.

During the same period, inhaled corticosteroid doses decreased about 20% among 96 patients who received the same inhaled corticosteroid throughout the first and second extensions and were not taking oral corticosteroids, reported Dr. Hébert, director of the Centre de Recherche Appliquée en Allergie, Quebec City. He has no financial interest in either of the study's sponsors.

Of the 178 patients who enrolled in the second extension, 134 (75%) had at least one adverse event, generally of mild or moderate severity. ■

# Asthma Medication Use Drops Following Tonsillectomy

BY MICHELE G.  
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MIAMI BEACH — Adenotonsillectomy in children with asthma is associated with a significant improvement in their symptoms, Dr. David E. Karas reported in a poster presented at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

All of the children in Dr. Karas' prospective study received their surgery for usual indications, including chronic tonsillitis and obstructive sleep apnea. Nevertheless, by 1 year after their surgery, Dr. Karas said in an interview, many experienced significant decreases both in medication use

and asthma severity, while their parents reported missing many fewer days of work to care for children during asthma exacerbations.

"We're not saying get a tonsillectomy if you have asthma," said Dr. Karas, a pediatric otolaryngologist at Yale University, New Haven, Conn. "But it's clear that the surgery improves upper respiratory congestion and chronic sinusitis. When the upper airway is not doing well, that eventually takes a toll on the lower airway,



**'We're not saying get a tonsillectomy if you have asthma.' But it's clear that it improves congestion.**

DR. KARAS

and when we treat the upper airway, the lower airway can improve."

He enrolled 31 patients aged 2-12 years who underwent adenoidectomy and/or tonsillectomy and had a diagnosis of asthma. Before the surgery, each caregiver filled out a questionnaire asking about medication use, asthma severity, and school and work days missed because of asthma exacerbation. Caregivers were contacted a mean of 1 year later and asked the same questions.

Medication use dropped significantly after surgery. The number of patients using inhaled steroids decreased from 25 to 14, albuterol from 30 to 18, and leukotriene moderators from 16 to 11. The single patient who was taking a long-acting  $\beta_2$ -agonist before surgery was no

longer taking it afterward.

The use of systemic steroids decreased as well. Before surgery, 22 patients used the drugs at least once a year; 8 required one course, 5 required two courses, 3 required three courses, and 6 required four courses. After surgery, only eight patients were using systemic steroids; all required one or two courses.

Caregivers also reported an average decrease from 2.0 to 0.81 in asthma severity symptom scores. All classes of asthma severity decreased: The number of children with severe persistent asthma declined from 4 to 0, with moderate persistent from 6 to 2, with mild persistent from 7 to 3, and with mild intermittent from 14 to 13. At the 1-year follow-up, 13 caregivers reported that their child had no asthma symptoms at all.

Of those children who attend-

ed school, the average number of missed school days per year decreased from 12.5 to 6. Caregivers' missed work days decreased as well, from 13 to 2 per year.

The relationship between upper airway infection and lower airway dysfunction may explain why some children with asthma experience exacerbations during winter and fall, when upper respiratory infections are more common, and why their symptoms improve with both oral corticosteroids and antibiotics, Dr. Karas said. "There's nothing that shrinks the tonsils like steroids—it's like you're giving a temporary medical tonsillectomy. And antibiotics treat the infective component by preventing those infected secretions that might be micro-aspirated and start up a reactive airway process." ■